IN THE CLAIMS:

Please amend claim 22 and add new claims 33-38.

This listing of claims will replace all prior versions, and listings of the claims in the application.

Listing of the claims

1.–11. **(Canceled).**

12.   **(Previously presented)**   A method of generating a microRNA comprising the steps of:

identifying a selected mRNA sequence to be the target of the microRNA; and

generating an oligonucleotide sequence that is 17-25 nucleotides and has a degree of complementarity to the selected mRNA sequence that is indicative of a microRNA-recognition element for a microRNA wherein the microRNA includes

a proximal region that is 7-9 nucleotides, has a 5' end and a 3' end and includes a nucleotide at the 5' end which is the microRNA's 5' terminus nucleotide,

a distal region that is 7-15 nucleotides, has a 5' end and a 3' end and includes a nucleotide at the 3' end which is the microRNA's 3' terminus nucleotide, and

a loop region that is 0 nucleotides, 2-3 nucleotides, or 6-9 nucleotides,

wherein when the loop region is 0 nucleotides, the 3' end of the proximal region is contiguous to the 5' end of the distal region, and when the loop region is 2-3 nucleotides or 6-9 nucleotides, the 3' end of the proximal region is contiguous to the 5' end of the loop region, and the 3' end of the loop region is contiguous to the 5' end of the distal region,

wherein complementarity of the mRNA sequence to the microRNA sequence that is indicative of a microRNA-response element for the microRNA is characterized by:

an mRNA sequence having a sequence that:

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       a)   includes a-region corresponding to the proximal region of the microRNA that is either: (i) completely complementary to the proximal region, or (ii) has a single mismatch (A) to the 5' end of the proximal region, or (B) symmetrically placed between the 5' end of the proximal region and the 3' end of the proximal region; and

       b)   includes a region corresponding to the loop region of the microRNA that either forms a loop of 2-5 non-paired nucleotides of mRNA when the loop region of the microRNA is 0, or the mRNA has 0 nucleotides when the loop region of the microRNA is 6-9 nucleotides, or the mRNA has 2-3 nucleotides which forms a bulge of 2-3 non-complementary nucleotides of mRNA when the loop region of the microRNA is 2-3 nucleotides; and

       c)   includes a region corresponding to the distal region of the microRNA that is either: (i) completely complementary to at least 7 contiguous nucleotides of the distal region of the microRNA, including the 5' end of the distal region, or (ii) contains (A) mismatches of 1-4 contiguous nucleotides and (B) matches of at least 5 nucleotides to a contiguous nucleotide sequence of the distal region of the microRNA, including the 5' end of the distal region;

    wherein the oligonucleotide sequence has a degree of complementarity to the selected mRNA sequence that is indicative of a microRNA for a microRNA-recognition element.

13.   **(Original)**   The method of claim 12 further comprising the step of determining free energy of the microRNA bound to the selected mRNA sequence wherein a free energy determination of -10 kcal/mole or less indicates that said mRNA sequence is a microRNA-recognition element for the microRNA.

14.   **(Original)**   The method of claim 12 wherein a free energy determination of -20 kcal/mole or less indicates that said mRNA sequence is a microRNA-recognition element for the microRNA.

15. **(Original)** The method of claim 12 wherein a free energy determination of -30 kcal/mole or less indicates that said mRNA sequence is a microRNA-recognition element for the microRNA.

16. **(Previously presented)** The method of claims 12 wherein the selected mRNA sequence is a known MRE.

17. **(Previously presented)** The method of claims 12 wherein the selected mRNA sequence is in the 3' untranslated region of an mRNA.

18. **(Previously presented)** The method of claims 12 wherein an oligonucleotide is synthesized having the sequence of the generated microRNA.

19. **(Previously presented)** A system for identifying a microRNA-recognition element comprising:

an input interface for inputting mRNA sequences, a database of mRNA sequences or a link for connecting to a remote data input interface, data or a database of mRNA sequences;

an input interface for inputting microRNA sequences, a database of microRNA sequences or a link for connecting to a remote data input interface, data or a database of microRNA sequences;

a processor with instructions for comparing mRNA sequences to microRNA sequences to identify a microRNA-recognition element according to the method of claims 12.

20. **(Previously presented)** The system of claim 19 comprising a link for connecting to a database of mRNA sequences.

21. **(Previously presented)** The system of claim 19 comprising an input interface for inputting microRNA sequences.

22.   (Currently amended)   A computer program embodied on a computer readable medium for implementation on a computer system that ~~for~~ identifying a microRNA-~~recognition element~~oligonucletide sequence, the program comprising instructions for performing the steps of the method of claim[s] 12.

23.–26. (Canceled).

27.   (Previously presented)   The method of claim 12, further comprising the step of synthesizing the oligonucleotide sequence and testing the function of the oligonucleotide to determine whether the oligonucleotide modulates the expression of the mRNA.

28.   (Previously presented)   The method of claim 27, wherein the step of testing the function of the microRNA results in activation or inhibition of the expression of the mRNA by at least 10%.

29.   (Previously presented)   A method of preparing a microRNA comprising the step of:

confirming that a microRNA candidate oligonucleotide functions to inhibit expression of a selected mRNA sequence that is present in a cell by contacting the microRNA candidate oligonucleotide with the selected mRNA present in the cell and determining expression;

wherein said microRNA candidate oligonucleotide was produced by

a) identifying a selected mRNA sequence that is present in a cell to be the target of the microRNA candidate;

b) generating an oligonucleotide sequence of a microRNA candidate oligonucleotide, wherein the oligonucleotide sequence is

1) 17-25 nucleotides, and

2) has a degree of complementarity to the selected mRNA sequence that is indicative of a microRNA-recognition element for a microRNA,

wherein the 17-25 nucleotides of the microRNA candidate include

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i) a proximal region that is 7-9 nucleotides, has a 5' end and a 3' end and includes a nucleotide at the 5' end which is the microRNA candidate's 5' terminus nucleotide,

ii) a distal region that is 7-15 nucleotides, has a 5' end and a 3' end and includes a nucleotide at the 3' end which is the microRNA candidate's 3' terminus nucleotide, and

iii) a loop region that is 0 nucleotides, 2-3 nucleotides or 6-9 nucleotides,

wherein

when the loop region of the microRNA candidate is 0 nucleotides, the 3' end of the proximal region is contiguous to the 5' end of the distal region, and

when the loop region of the microRNA candidate is 2-3 nucleotides or 6-9 nucleotides, the 3' end of the proximal region is contiguous to the 5' end of the loop region and the 3' end of the loop region is contiguous to the 5' end of the distal region,

and

wherein complementarity of the mRNA sequence to the microRNA candidate sequence that is indicative of a microRNA-response element for the microRNA candidate is characterized by an mRNA sequence having a sequence that:

i) includes a region in the mRNA sequence corresponding to the proximal region of the microRNA candidate that is either

A) completely complementary to the proximal region of the microRNA candidate, or

B) has a single mismatch to the 5' end of the proximal region of the microRNA candidate, or

        C) has a single mismatch symmetrically between the 5' end of the proximal region of the microRNA candidate and the 3' end of the proximal region of the microRNA candidate;

    ii) includes a region in the mRNA sequence corresponding to the loop region of the microRNA candidate that either

        A) forms a loop of 2-5 non-paired nucleotides of mRNA when the loop region of the microRNA candidate is 0, or

        B) has 0 nucleotides of mRNA sequence when the loop region of the microRNA candidate is 6-9 nucleotides, or

        C) has 2-3 nucleotides in the mRNA sequence which form a bulge of 2-3 non-complementary nucleotides in the mRNA sequence when the loop region of the microRNA candidate is 2-3 nucleotides; and

    iii) includes a region corresponding to the distal region that is either:

        (A) completely complementary to at least 7 contiguous nucleotides of the distal region of the microRNA candidate including the 5' end of the distal region of the microRNA candidate, or

        (B) contains (i) mismatches of 1-4 contiguous nucleotides of mRNA sequence and (ii) matches of at least 5 nucleotides of mRNA sequence to a contiguous nucleotide sequence of the distal region of the microRNA candidate including the 5' end of the distal region of the microRNA candidate;

and

    c) synthesizing a microRNA candidate oligonucleotide having said oligonucleotide sequence.

30.   **(Previously Presented)**   The method of claim 29 wherein contacting the microRNA candidate oligonucleotide with the selected mRNA present in the cell results in inhibition of the expression of the mRNA by at least 10%.

31.   **(Previously Presented)**   The method of claim 12, wherein in step b) the mRNA includes a region corresponding to the loop region of the microRNA that forms a loop of 2-5 non-paired nucleotides of mRNA when the loop region of the microRNA is 0.

32.   **(Previously Presented)**   The method of claim 12, wherein in step b) the mRNA includes a region corresponding to the loop region of the microRNA, wherein said region of mRNA has 0 nucleotides when the loop region of the microRNA is 6-9 nucleotides.

33.   **(New)**   A method of preparing a microRNA comprising the steps of:

identifying a selected mRNA sequence to be the target of the microRNA;

generating a microRNA oligonucleotide sequence that is 17-25 nucleotides, wherein the selected mRNA sequence has a degree of complementarity to the microRNA oligonucleotide sequence that is indicative of a microRNA-recognition element for a microRNA having the microRNA oligonucleotide sequence,

wherein the microRNA oligonucleotide sequence includes

a microRNA proximal region that is 7-9 nucleotides, has a 5' end and a 3' end and includes a nucleotide at the 5' end which is the microRNA's 5' terminus nucleotide,

a microRNA distal region that is 7-15 nucleotides, has a 5' end and a 3' end and includes a nucleotide at the 3' end which is the microRNA's 3' terminus nucleotide, and

a microRNA loop region that is 0 nucleotides, 2-3 nucleotides, or 6-9 nucleotides,

wherein when the microRNA loop region is 0 nucleotides, the 3' end of the microRNA proximal region is contiguous to the 5' end of the microRNA distal region, and when the microRNA loop region is 2-3 nucleotides or 6-9 nucleotides, the 3' end of the microRNA proximal region is contiguous to the 5' end of the microRNA loop region, and the 3' end of the microRNA loop region is contiguous to the 5' end of the microRNA distal region,

wherein complementarity of the mRNA sequence to the microRNA oligonucleotide sequence that is indicative of a microRNA-response element for the microRNA is characterized by:

an mRNA sequence having a sequence that:

a)   includes an mRNA region corresponding to the microRNA proximal region of the microRNA that is either: (i) completely complementary to the microRNA proximal region, or (ii) has a single mismatch (A) to the 5' end of the microRNA proximal region, or (B) symmetrically placed between the 5' end of the microRNA proximal region and the 3' end of the microRNA proximal region; and

b)   includes an mRNA region corresponding to the microRNA loop region of the microRNA that either forms an mRNA loop of 2-5 non-paired nucleotides of mRNA when the microRNA loop region of the microRNA is 0, or the mRNA region corresponding to the microRNA loop region of the microRNA has 0 nucleotides when the microRNA loop region of the microRNA is 6-9 nucleotides, or the mRNA region corresponding to the microRNA loop region of the microRNA has 2-3 nucleotides which forms a bulge of 2-3 non-complementary nucleotides of mRNA when the microRNA loop region of the microRNA is 2-3 nucleotides; and

c)   includes an mRNA region corresponding to the microRNA distal region of the microRNA that is either: (i) completely complementary to at least 7 contiguous nucleotides of the microRNA distal region of the microRNA, including the 5' end of the

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microRNA distal region, or (ii) contains (A) mismatches of 1-4 contiguous nucleotides and (B) matches of at least 5 nucleotides to a contiguous nucleotide sequence of the microRNA distal region of the microRNA, including the 5' end of the microRNA distal region;

determining free energy of a microRNA having the microRNA oligonucleotide sequence bound to the selected mRNA sequence wherein a free energy determination of -10 kcal/mole or less indicates that said mRNA sequence is a microRNA-recognition element for the microRNA having the microRNA oligonucleotide sequence; and

synthesizing a nucleic acid molecule, wherein the nucleotide sequence of the nucleic acid molecule is the microRNA oligonucleotide sequence.

34.   (New)   The method of claim 33 wherein a free energy determination of -20 kcal/mole or less indicates that said mRNA sequence is a microRNA-recognition element for the microRNA.

35.   (New)   The method of claim 33 wherein a free energy determination of -30 kcal/mole or less indicates that said mRNA sequence is a microRNA-recognition element for the microRNA.

36.   (New)   The method of claims 33 wherein the selected mRNA sequence is in the 3' untranslated region of an mRNA.

37.   (New)   The method of claim 33 further comprising the step of testing the function of the oligonucleotide to determine whether the oligonucleotide modulates the expression of the mRNA.

38.   (New)   The method of claim 33, wherein the step of testing the function of the microRNA results in activation or inhibition of the expression of the mRNA by at least 10%.

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